

Hypercalcemia due to hyperparathyroidism treated with a somatostatin analogue

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Treatment of life-threatening hypercalcemia (serum calcium level greater than 3.25 mmol/L) is ideally directed at the primary cause (usually malignant disease or hyperparathyroidism),¹ but since surgery is risky when the serum calcium level is very high the level should first be lowered medically.² The somatostatin analogue octreotide (Sandostatin, Sandoz Canada Inc., Dorval, Que.) has recently been reported to be effective in the treatment of hypercalcemia due to malignant disease.^{3,4} Unlike some of the other drugs used to lower serum calcium levels, octreotide is readily available, easy to administer and relatively free of side effects. We describe its use in a patient with hyperparathyroidism and severe hypercalcemia.

Case report

A 73-year-old woman, described by her family as having recently become more somnolent and paranoid, presented to the emergency department complaining of light-headedness, nausea, vomiting and constipation of several weeks' duration. A daughter had undergone surgery for parathyroid hyperplasia. The patient was confused and drowsy; she was also dehydrated and had a diffusely tender abdomen. The serum level of calcium was 3.98 mmol/L, of phosphate 0.85 mmol/L, of albumin 39 g/L and of creatinine 103 µmol/L.

The patient's severe hypercalcemia made immediate surgery too risky. Rehydration and forced diuresis (an average of 14 L/d) had little effect on the confusion and drowsiness or on the serum calcium level. The subcutaneous administration of octreotide, 50 µg every 12 hours, returned the serum calcium level to normal and suppressed the serum

parathormone (PTH) level (Table 1). A subsequent recurrence of hypercalcemia responded to octreotide, 100 µg every 12 hours, and elemental phosphate, 3 g/d orally. Although the patient's confusion and drowsiness resolved, the course of the illness was complicated by a deep-vein thrombosis in the left common iliac vein 8 days after admission; intravenous heparin therapy and an inferior vena cava filter were used to treat the thrombus.

Ultrasonography of the neck and a parathyroid subtraction scan revealed a mass near the inferior pole of the right lobe of the thyroid. On the 22nd day

Table 1: Effect of octreotide on serum parathormone (PTH) level as measured by two assays in a woman with hypercalcemia

Date	Dose, µg every 12 hours	Assay; PTH level, ng/L	
		MM PTH*	Intact PTH†
July 14	—	25 590	678
15	—	24 490	604
17	50	—	—
19	50	20 970	447
21	50	17 020	—
25	100	16 200	—
26	100	14 200	367
27	100	15 130	363
Aug 3‡	—	15 300	356
9	—	3 587	196
13	—	5 357	191
15	—	4 474	232

*Mid-molecule PTH assay (PTH-MM RIA, Incstar Corporation, Stillwater, Minn.); normal limits are 290 and 850 ng/L.

†Intact PTH assay (Allegro Intact PTH [IRMA] Immunoassay, Nichols Institute Diagnostics, San Juan Capistrano, Calif.); normal limits are 10 and 65 ng/L.

‡Right inferior parathyroidectomy performed.

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the patient underwent surgery. Because of her poor (although improved) general condition this was limited to the right inferior parathyroid; a mass $4 \times 2.2 \times 1.3$ cm was excised. The results of pathological studies indicated that the mass was a parathyroid adenoma.

The patient's hospital course is depicted in Fig. 1. Because the serum albumin level fell postoperatively the serum calcium level was corrected by adding 0.02 mmol/L for each 1 g/L decrease in the albumin level below 40 g/L. The PTH level was measured by a mid-molecule PTH assay (PTH-MM RIA, Incstar Corporation, Stillwater, Minn.) and an intact PTH assay (Allegro Intact PTH [IRMA] Immunoassay, Nichols Institute Diagnostics, San Juan Capistrano, Calif.). The octreotide and phosphate therapies were discontinued after surgery, and the serum calcium level remained at or slightly above normal. Although still elevated the intact PTH level decreased by one-third and the mid-molecule PTH level by more than two-thirds of the immediate preoperative value. The postoperative course was uneventful, and the patient was discharged home 12 days after surgery.

Comments

Successful preoperative control of this patient's hypercalcemia was achieved by means of the somatostatin analogue octreotide. Recent articles have reported on the successful use of octreotide for hypercalcemia associated with a pheochromocytoma³ and a pancreatic islet cell tumour.⁴ In both cases there was an elevated level of PTH-related peptide (PHRP), which in the former case dropped significantly during octreotide therapy.

Octreotide has also been found to suppress

levels of peptide hormones elevated by a number of functional endocrine tumours of the gastrointestinal tract.⁵ In the present case the stepwise reduction in the serum PTH level with changes in the octreotide dose did not appear to be sufficiently great to explain the resulting "normocalcemia." Whether octreotide has additional uses, such as the inhibition of osteoclasts, cannot be determined at this time.

Sandoz Canada Inc. has indicated that there is only one other report of thrombophlebitis associated with the use of octreotide, but this occurred in a patient with pancreatitis and dehydration — known causes of thrombophlebitis (personal communication). Our patient was similarly predisposed.

Our patient's serum PTH level did not return to normal even after surgery. Persistently elevated PTH levels along with a return to normal of the serum calcium level have been reported after the removal of parathyroid adenomas.⁶ Possible causes include the presence of parathyroid hyperplasia rather than an adenoma, renal impairment or "bone hunger" for calcium, which decreases the serum calcium level and stimulates PTH release transiently (for several weeks or months) from the remaining glands. Despite the presence of one large gland the possibility of parathyroid hyperplasia would be supported in this case by the family history and the slightly, but persistently, elevated postoperative serum calcium level.

Octreotide appears to be safe and effective in controlling hypercalcemia due to excess amounts of PTH and PHRP. Because the drug is readily available and easy to administer it may be an ideal agent in the immediate management of severe hypercalcemia. Further studies are needed to determine whether octreotide has an accepted role in the treatment of hypercalcemia due to malignant disease or hyperparathyroidism.

References

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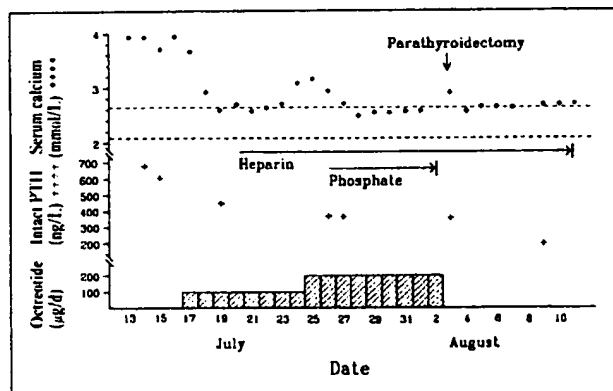


Fig. 1: Effect on serum calcium level (normal range shown by broken lines) and intact parathormone (PTH) level (normal range 10 to 65 ng/L) of rehydration and forced diuresis (July 13 to 16), octreotide (100 and 200 μ g/d) and surgical removal of tumour in right inferior parathyroid gland.